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<120> Feedback-resistant mevalonate kinases

<130> Case 21788

<150> EP 03012294.9

<151> 2003-06-12

<160> 33

<170> PatentIn version 3.2

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Met Ala Ile Ala Arg Tyr Thr Glu Val Trp Phe Thr Pro Leu Gly Ile 35 40 45

Gly Glu Gly Ile Arg Thr Thr Phe Ala Asn Leu Ser Gly Gly Ala Thr 50 60

Tyr Ser Leu Lys Leu Leu Ser Gly Phe Lys Ser Arg Leu Asp Arg Arg 65 70 75 80

Phe Glu Gln Phe Leu Asn Gly Asp Leu Lys Val His Lys Val Leu Thr 85 90 95

His Pro Asp Asp Leu Ala Val Tyr Ala Leu Ala Ser Leu Leu His Asp $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$

Lys Pro Pro Gly Thr Ala Ala Met Pro Gly Ile Gly Ala Met His His 115 120 125

Leu Pro Arg Pro Gly Glu Leu Gly Ser Arg Thr Glu Leu Pro Ile Gly 130 135 140

Ala Gly Met Gly Ser Ser Ala Ala Ile Val Ala Ala Thr Thr Val Leu 145 150 155 160

Phe Glu Thr Leu Leu Asp Arg Pro Lys Thr Pro Glu Gln Arg Phe Asp Page 1 Arg Val Arg Phe Cys Glu Arg Leu Lys His Gly Lys Ala Gly Pro Ile 180

Asp Ala Ala Ser Val Val Arg Gly Gly Leu Val Arg Val Gly Gly Asn 200

Gly Pro Gly Ser Ile Ser Ser Phe Asp Leu Pro Glu Asp His Asp Leu 210 215 220

Val Ala Gly Arg Gly Trp Tyr Trp Val Leu His Gly Arg Pro Val Ser 235 230 235

Gly Thr Gly Glu Cys Val Ser Ala Val Ala Ala Ala His Gly Arg Asp 245 250 255

Ala Ala Leu Trp Asp Ala Phe Ala Val Cys Thr Arg Ala Leu Glu Ala 260 265 270

Ala Leu Leu Ser Gly Gly Ser Pro Asp Ala Ala Ile Thr Glu Asn Gln 275 280 285

Arg Leu Leu Glu Arg Ile Gly Val Val Pro Ala Ala Thr Gln Ala Leu 290 295 300

Val Ala Gln Ile Glu Glu Ala Gly Gly Ala Ala Lys Ile Cys Gly Ala 305 310 315 320

Gly Ser Val Arg Gly Asp His Gly Gly Ala Val Leu Val Arg Ile Asp 325 330 335

Asp Ala Gln Ala Met Ala Ser Val Met Ala Arg His Pro Asp Leu Asp 340 345 350

Trp Ala Pro Leu Arg Met Ser Arg Thr Gly Ala Ala Pro Gly Pro Ala 355 360 365

Pro Arg Ala Gln Pro Leu Pro Gly Gln Gly 370

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<211> 396 <212> PRT

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Met Leu Ser Glu Val Leu Leu Val Ser Ala Pro Gly Lys Val Ile Leu Page 2 5

1

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35 40 45 Val Asp Leu Ser Leu Pro Asn Ile Gly Ile Lys Arg Ala Trp Asp Val 50 55 60 Ala Arg Leu Gln Ser Leu Asp Thr Ser Phe Leu Glu Gln Gly Asp Val 65 70 75 80 Thr Thr Pro Thr Ser Glu Gln Val Glu Lys Leu Lys Glu Val Ala Gly 85 90 95 Leu Pro Asp Asp Cys Ala Val Thr Glu Arg Leu Ala Val Leu Ala Phe 100 105 110 Leu Tyr Leu Tyr Leu Ser Ile Cys Arg Lys Gln Arg Ala Leu Pro Ser 115 120 125 Leu Asp Ile Val Val Trp Ser Glu Leu Pro Pro Gly Ala Gly Leu Gly 130 140 Ser Ser Ala Ala Tyr Ser Val Cys Leu Ala Ala Ala Leu Leu Thr Val 145 150 155 160 Cys Glu Glu Ile Pro Asn Pro Leu Lys Asp Gly Asp Cys Val Asn Arg 165 170 175 Trp Thr Lys Glu Asp Leu Glu Leu Ile Asn Lys Trp Ala Phe Gln Gly 180 185 190 Glu Arg Met Ile His Gly Asn Pro Ser Gly Val Asp Asn Ala Val Ser 195 200 205 Thr Trp Gly Gly Ala Leu Arg Tyr His Gln Gly Lys Ile Ser Ser Leu 210 220 Lys Arg Ser Pro Ala Leu Gln Ile Leu Leu Thr Asn Thr Lys Val Pro 235 230 240

Arg Asn Thr Arg Ala Leu Val Ala Gly Val Arg Asn Arg Leu Leu Lys 245 250 255

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Val Ser Val Asn Leu Pro Asn Ile Gly Ile Lys Gln Val Trp Asp Val 50 60

Gly Met Leu Gln Arg Leu Asp Thr Ser Phe Leu Glu Gln Gly Asp Val 70 75 80

21788wo.ST25.txt Ser Val Pro Thr Leu Glu Gln Leu Glu Lys Leu Lys Lys Met Gly Asp 85 90 95 Leu Pro Arg Asp Arg Ala Gly Asn Glu Gly Met Ala Leu Leu Ala Phe 100 105 110 Leu Tyr Leu Tyr Leu Ala Ile Cys Arg Lys Gln Arg Thr Leu Pro Ser 115 120 125 Leu Asp Met Val Val Trp Ser Glu Leu Pro Pro Gly Ala Gly Leu Gly 130 135 140 Ser Ser Ala Ala Tyr Ser Val Cys Leu Ala Ala Ala Leu Leu Thr Ala 145 150 155 160 Cys Glu Glu Val Ser Asn Pro Leu Lys Asp Gly Val Ser Val Ser Arg 165 170 175 Trp Pro Glu Glu Asp Leu Lys Ser Ile Asn Lys Trp Ala Phe Glu Gly
180 185 190 Glu Arg Val Ile His Gly Asn Pro Ser Gly Val Asp Asn Ala Val Ser 195 200 205 Thr Trp Gly Gly Ala Leu Arg Phe Gln Gln Gly Thr Met Ser Ser Leu 210 220 Lys Ser Leu Pro Ser Leu Gln Ile Leu Leu Thr Asn Thr Lys Val Pro 225 230 235 240 Arg Ser Thr Lys Ala Leu Val Ala Ala Val Arg Ser Arg Leu Thr Lys 245 250 255 Phe Pro Glu Ile Val Ala Pro Leu Leu Thr Ser Ile Asp Ala Ile Ser 260 265 270 Leu Glu Cys Glu Arg Val Leu Gly Glu Met Val Ala Ala Pro Val Pro 275 280 285 Glu Gln Tyr Leu Val Leu Glu Glu Leu Ile Asp Met Asn Gln His His 290 295 300 Leu Asn Ala Leu Gly Val Gly His Asn Ser Leu Asp Gln Leu Cys Gln 305 310 315 320

Val Thr Ala Ala His Gly Leu His Ser Lys Leu Thr Gly Ala Gly Gly 325 330 . 335

Gly Gly Cys Gly Ile Thr Leu Leu Lys Pro Gly Leu Glu Gln Ala Thr 340 345 350

Val Glu Ala Ala Lys Gln Ala Leu Thr Ser Cys Gly Phe Asp Cys Trp 355 360 365

Glu Thr Ser Ile Gly Ala Pro Gly Val Ser Thr His Ser Ala Ala Ala 370 375 380

Val Gly Asp Pro Val Arg Gln Ala Leu Gly Leu 385 390 395

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35 40 45

Val Ser Leu Asn Leu Pro Asn Val Gly Ile Lys Gln Val Trp Asp Val 50 60

Ala Thr Leu Gln Leu Leu Asp Thr Gly Phe Leu Glu Gln Gly Asp Val 65 70 75 80

Pro Ala Pro Thr Leu Glu Glu Lus Lus Lus Lus Val Ala Gly 85 90 95

Leu Pro Arg Asp Cys Val Gly Asn Glu Gly Leu Ser Leu Leu Ala Phe 100 105 110

Leu Tyr Leu Tyr Leu Ala Ile Cys Arg Lys Gln Arg Thr Leu Pro Ser 115 120 125

Leu Asp Ile Met Val Trp Ser Glu Leu Pro Pro Gly Ala Gly Leu Gly 130 140

Ser Ser Ala Ala Tyr Ser Val Cys Val Ala Ala Ala Leu Leu Thr Ala 145 150 155 160

Cys Glu Glu Val Thr Asn Pro Leu Lys Asp Arg Gly Ser Ile Gly Ser 165 170 175

Trp Pro Glu Glu Asp Leu Lys Ser Ile Asn Lys Trp Ala Tyr Glu Gly 180 185 190

Glu Arg Val Ile His Gly Asn Pro Ser Gly Val Asp Asn Ser Val Ser 195 200 205

Thr Trp Gly Gly Ala Leu Arg Tyr Gln Gln Gly Lys Met Ser Ser Leu 210 220

Lys Arg Leu Pro Ala Leu Gln Ile Leu Leu Thr Asn Thr Lys Val Pro 225 230 235 240

Arg Ser Thr Lys Ala Leu Val Ala Gly Val Arg Ser Arg Leu Ile Lys 245 250 255

Phe Pro Glu Ile Met Ala Pro Leu Leu Thr Ser Ile Asp Ala Ile Ser 260 265 270

Leu Glu Cys Glu Arg Val Leu Gly Glu Met Ala Ala Ala Pro Val Pro 275 280 285

Glu Gln Tyr Leu Val Leu Glu Glu Leu Met Asp Met Asn Gln His His 290 295 300

Leu Asn Ala Leu Gly Val Gly His Ala Ser Leu Asp Gln Leu Cys Gln 305 310 315 320

Val Thr Ala Ala His Gly Leu His Ser Lys Leu Thr Gly Ala Gly Gly 325 330 335

Gly Gly Cys Gly Ile Thr Leu Leu Lys Pro Gly Leu Glu Arg Ala Lys 340 350

Val Glu Ala Ala Lys Gln Ala Leu Thr Gly Cys Gly Phe Asp Cys Trp 355 360 365

Glu Thr Ser Ile Gly Ala Pro Gly Val Ser Met His Ser Ala Thr Ser 370 380

Ile Glu Asp Pro Val Arg Gln Ala Leu Gly Leu 385 390 395

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<213> Arabidopsis thaliana

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Tyr Thr Tyr Val Thr Leu Arg Phe Pro Leu Pro Ser Ala Glu Asn Asn 35 40 45

Asp Arg Leu Thr Leu Gln Leu Lys Asp Ile Ser Leu Glu Phe Ser Trp 50 60

Ser Leu Ala Arg Ile Lys Glu Ala Ile Pro Tyr Asp Ser Ser Thr Leu 65 70 75 80

Cys Arg Ser Thr Pro Ala Ser Cys Ser Glu Glu Thr Leu Lys Ser Ile 85 90 95

Ala Val Leu Val Glu Glu Gln Asn Leu Pro Lys Glu Lys Met Trp Leu 100 105 110

Ser Ser Gly Ile Ser Thr Phe Leu Trp Leu Tyr Thr Arg Ile Ile Gly 115 120 125

Phe Asn Pro Ala Thr Val Val Ile Asn Ser Glu Leu Pro Tyr Gly Ser 130 135 140

Gly Leu Gly Ser Ser Ala Ala Leu Cys Val Ala Leu Thr Ala Ala Leu 145 150 155 160

Leu Ala Ser Ser Ile Ser Glu Lys Thr Arg Gly Asn Gly Trp Ser Ser 165 170 175

Leu Asp Glu Thr Asn Leu Glu Leu Leu Asn Lys Trp Ala Phe Glu Gly 180 185 190

Glu Lys Ile Ile His Gly Lys Pro Ser Gly Ile Asp Asn Thr Val Ser 195 200 205

Ala Tyr Gly Asn Met Ile Lys Phe Cys Ser Gly Glu Ile Thr Arg Leu 210 215 220

Gln Ser Asn Met Pro Leu Arg Met Leu Ile Thr Asn Thr Arg Val Gly 235 240 Page 8

Arg Asn Thr Lys Ala Leu Val Ser Gly Val Ser Gln Arg Ala Val Arg 245 250 255

His Pro Asp Ala Met Lys Ser Val Phe Asn Ala Val Asp Ser Ile Ser 260 265 270

Lys Glu Leu Ala Ala Ile Ile Gln Ser Lys Asp Glu Thr Ser Val Thr 275 280 285

Glu Lys Glu Glu Arg Ile Lys Glu Leu Met Glu Met Asn Gln Gly Leu 290 295 300

Leu Leu Ser Met Gly Val Ser His Ser Ser Ile Glu Ala Val Ile Leu 305 310 315 320

Thr Thr Val Lys His Lys Leu Val Ser Lys Leu Thr Gly Ala Gly Gly 325 330 335

Gly Gly Cys Val Leu Thr Leu Leu Pro Thr Gly Thr Val Val Asp Lys 340 345 350

Val Val Glu Glu Leu Glu Ser Ser Gly Phe Gln Cys Phe Thr Ala Leu 355 360 365

Ile Gly Gly Asn Gly Ala Gln Ile Cys Tyr 370 375

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<211> 443

<212> PRT

<213> Saccharomyces cerevisiae

<400> 6

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Gly Glu His Ser Ala Val Tyr Asn Lys Pro Ala Val Ala Ala Ser Val 20 25 30

Ser Ala Leu Arg Thr Tyr Leu Leu Ile Ser Glu Ser Ser Ala Pro Asp 35 40 45

Thr Ile Glu Leu Asp Phe Pro Asp Ile Ser Phe Asn His Lys Trp Ser 50 60

Ile Asn Asp Phe Asn Ala Ile Thr Glu Asp Gln Val Asn Ser Gln Lys
65 70 75 80
Page 9

Leu Ala Lys Ala Gln Gln Ala Thr Asp Gly Leu Ser Gln Glu Leu Val 85 90 95 Ser Leu Leu Asp Pro Leu Leu Ala Gln Leu Ser Glu Ser Phe His Tyr $100 \hspace{1cm} 105 \hspace{1cm} 110$ His Ala Ala Phe Cys Phe Leu Tyr Met Phe Val Cys Leu Cys Pro His 115 120 125 Ala Lys Asn Ile Lys Phe Ser Leu Lys Ser Thr Leu Pro Ile Gly Ala 130 135 140 Gly Leu Gly Ser Ser Ala Ser Ile Ser Val Ser Leu Ala Leu Ala Met 145 150 155 160 Ala Tyr Leu Gly Gly Leu Ile Gly Ser Asn Asp Leu Glu Lys Leu Ser 165 170 175 Glu Asn Asp Lys His Ile Val Asn Gln Trp Ala Phe Ile Gly Glu Lys 180 185 190 Cys Ile His Gly Thr Pro Ser Gly Ile Asp Asn Ala Val Ala Thr Tyr 195 200 205 Gly Asn Ala Leu Leu Phe Glu Lys Asp Ser His Asn Gly Thr Ile Asn 210 220 Thr Asn Asn Phe Lys Phe Leu Asp Asp Phe Pro Ala Ile Pro Met Ile 225 230 235 240 Leu Thr Tyr Thr Arg Ile Pro Arg Ser Thr Lys Asp Leu Val Ala Arg 245 250 255 Val Arg Val Leu Val Thr Glu Lys Phe Pro Glu Val Met Lys Pro Ile 260 265 270 Leu Asp Ala Met Gly Glu Cys Ala Leu Gln Gly Leu Glu Ile Met Thr 275 280 285 Lys Leu Ser Lys Cys Lys Gly Thr Asp Asp Glu Ala Val Glu Thr Asn 290 295 300 Asn Glu Leu Tyr Glu Gln Leu Leu Glu Leu Ile Arg Ile Asn His Gly 305 310 315 Leu Leu Val Ser Ile Gly Val Ser His Pro Gly Leu Glu Leu Ile Lys Page 10

Asn Leu Ser Asp Asp Leu Arg Ile Gly Ser Thr Lys Leu Thr Gly Ala 340 350

Gly Gly Gly Cys Ser Leu Thr Leu Leu Arg Arg Asp Ile Thr Gln 355 360

Glu Gln Ile Asp Ser Phe Lys Lys Leu Gln Asp Asp Phe Ser Tyr 370 375 380

Glu Thr Phe Glu Thr Asp Leu Gly Gly Thr Gly Cys Cys Leu Leu Ser 385 390 395 400

Ala Lys Asn Leu Asn Lys Asp Leu Lys Ile Lys Ser Leu Val Phe Gln 405 410 415

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Leu Pro Gly Asn Thr Asn Leu Pro Trp Thr Ser 435 440

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404 <211>

<212> **PRT** Schizosaccharomyces pombe

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Gly Glu His Ala Val Val Tyr Gly Ala Thr Ala Leu Ala Ala Ala Val 20 25 30

Leu Arg Ser Tyr Cys Lys Leu Gln Thr Thr Asn Asn Asn Glu Ile 35 40 45

Val Ile Val Met Ser Asp Ile Gly Thr Glu Arg Arg Trp Asn Leu Gln 50 60

Ser Leu Pro Trp Gln His Val Thr Val Glu Asn Val Gln His Pro Ala 65 70 75 80

Ser Ser Pro Asn Leu Asp Leu Leu Gln Gly Leu Gly Glu Leu Leu Lys 85 90 95

Asn Glu Glu Asn Gly Leu Ile His Ser Ala Met Leu Cys Thr Leu Tyr Page 11

110

Leu Phe Thr Ser Leu Ser Ser Pro Ser Gln Gly Cys Thr Leu Thr Ile 115 120 125 Ser Ser Gln Val Pro Leu Gly Ala Gly Leu Gly Ser Ser Ala Thr Ile 130 135 140 Ser Val Val Val Ala Thr Ser Leu Leu Leu Ala Phe Gly Asn Ile Glu 145 150 155 160 Pro Pro Ser Ser Asn Ser Leu Gln Asn Asn Lys Ala Leu Ala Leu Ile 165 170 175 Glu Ala Trp Ser Phe Leu Gly Glu Cys Cys Ile His Gly Thr Pro Ser 180 185 190 Gly Ile Asp Asn Ala Val Ala Thr Asn Gly Gly Leu Ile Ala Phe Arg 195 200 205 Lys Ala Thr Ala His Gln Ser Ala Met Lys Glu Phe Leu Lys Pro Lys 210 220 Asp Thr Leu Ser Val Met Ile Thr Asp Thr Lys Gln Pro Lys Ser Thr 225 230 235 240 Lys Lys Leu Val Gln Gly Val Phe Glu Leu Lys Glu Arg Leu Pro Thr 245 250 255 Val Ile Asp Ser Ile Ile Asp Ala Ile Asp Gly Ile Ser Lys Ser Ala 260 265 270 Val Leu Ala Leu Thr Ser Glu Ser Asp Lys Asn Ser Ser Ala Lys Lys 275 280 285 Leu Gly Glu Phe Ile Val Leu Asn Gln Lys Leu Leu Glu Cys Leu Gly 290 295 300 Val Ser His Tyr Ser Ile Asp Arg Val Leu Gln Ala Thr Lys Ser Ile 305 310 315 320 Gly Trp Thr Lys Leu Thr Gly Ala Gly Gly Gly Gly Cys Thr Ile Thr 325 330 335 Leu Leu Thr Pro Glu Cys Lys Glu Glu Glu Phe Lys Leu Cys Lys Glu 340 350

21788wo.ST25.txt Ser Leu Leu Ala His Lys Asn Ser Ile Tyr Asp Val Gln Leu Gly Gly 360

Pro Gly Val Ser Val Val Thr Asp Ser Asp Ser Phe Phe Pro Gln Tyr 370 380

Glu Ser Asp Phe Asp Phe Lys Lys Leu Asn Leu Leu Ser Lys Phe Asn 395

Lys Tyr Tyr Ile

<210> <211> 335

<212> PRT

Pyrococcus abyssi

<400>

Met Pro Arg Leu Val Leu Ala Ser Ala Pro Ala Lys Ile Ile Leu Phe $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Gly Glu His Ser Val Val Tyr Gly Lys Pro Ala Ile Ala Ser Ala Ile 20 25 30

Asp Leu Arg Thr Tyr Val Arg Ala Glu Phe Asn Asp Ser Gly Asn Ile 35 40 45

Lys Ile Glu Ala His Asp Ile Lys Thr Pro Gly Leu Ile Val Ser Phe 50 60

Ser Glu Asp Lys Ile Tyr Phe Glu Thr Asp Tyr Gly Lys Ala Ala Glu 65 70 75 80

Val Leu Ser Tyr Val Arg His Ala Ile Glu Leu Val Leu Glu Glu Ala 85 90 95

Asp Lys Arg Thr Gly Val Ser Val Ser Ile Thr Ser Gln Ile Pro Val 100 105 110

Gly Ala Gly Leu Gly Ser Ser Ala Ala Val Ala Val Ala Thr Ile Gly 115 120 125

Ala Val Ser Lys Leu Leu Asp Leu Glu Leu Ser Lys Glu Glu Ile Ala 130 135 140

Lys Met Gly His Lys Val Glu Leu Leu Val Gln Gly Ala Ser Ser Gly 145 150 155 160

21788wo.ST25.txt Ile Asp Pro Thr Val Ser Ala Ile Gly Gly Phe Leu Tyr Tyr Lys Gln
165 170 175 Gly Glu Phe Glu His Leu Pro Phe Val Glu Leu Pro Ile Val Val Gly 180 185 190 Tyr Thr Gly Ser Ser Gly Ser Thr Lys Glu Leu Val Ala Met Val Arg 195 200 205 Arg Arg Tyr Glu Glu Met Pro Glu Leu Ile Glu Pro Ile Leu Glu Ser 210 215 220 Met Gly Lys Leu Val Asp Lys Ala Lys Glu Val Ile Ile Ser Lys Leu 225 230 235 240 Asp Glu Glu Lys Phe Leu Lys Leu Gly Glu Leu Met Asn Ile Asn 245 250 255 His Gly Leu Leu Asp Ala Leu Gly Val Ser Thr Lys Lys Leu Ser Glu 260 265 270 Leu Val Tyr Ala Ala Arg Thr Ala Gly Ala Ile Gly Ala Lys Leu Thr 275 280 285 Gly Ala Gly Gly Gly Cys Met Tyr Ala Leu Ala Pro Gly Lys Gln 290 295 300 Arg Glu Val Ala Thr Ala Ile Lys Ile Ala Gly Gly Thr Pro Met Ile 305 310 315 320 Thr Arg Ile Ser Lys Glu Gly Leu Arg Ile Glu Glu Val Arg Glu 325 330 335 <210> <211> 335 Pyrococcus horikoshii <400> 9 Met Val Lys Tyr Val Leu Ala Ser Ala Pro Ala Lys Val Ile Leu Phe 1 5 10 15 Gly Glu His Ser Val Val Tyr Gly Lys Pro Ala Ile Ala Ser Ala Ile 20 25 30 Glu Leu Arg Thr Tyr Val Arg Ala Gln Phe Asn Asp Ser Gly Asn Ile 35 40 45

21788wo.ST25.txt
Lys Ile Glu Ala His Asp Ile Lys Thr Pro Gly Leu Ile Val Ser Phe
50 55 60 Ser Glu Asp Lys Ile Tyr Phe Glu Thr Asp Tyr Gly Lys Ala Ala Glu 65 70 75 80 Val Leu Ser Tyr Val Arg Tyr Ala Ile Glu Leu Ala Leu Glu Glu Ser 85 90 95 Asp Lys Arg Val Gly Ile Asp Val Ser Ile Thr Ser Gln Ile Pro Val 100 105 110 Gly Ala Gly Leu Gly Ser Ser Ala Ala Val Ala Val Ala Thr Ile Gly 125 Ala Val Ser Arg Leu Leu Gly Leu Glu Leu Ser Lys Glu Glu Ile Ala 130 135 140 Lys Leu Gly His Lys Val Glu Leu Leu Val Gln Gly Ala Ser Ser Gly 145 150 155 160 Ile Asp Pro Thr Val Ser Ala Val Gly Gly Phe Leu Tyr Tyr Lys Gln
165 170 175 Gly Lys Phe Glu Pro Leu Pro Phe Met Glu Leu Pro Ile Val Val Gly 180 185 190 Tyr Thr Gly Ser Thr Gly Ser Thr Lys Glu Leu Val Ala Met Val Arg 195 200 205 Lys Arg Tyr Glu Glu Met Pro Glu Leu Val Glu Pro Ile Leu Glu Ala 210 215 220 Met Gly Lys Leu Val Asp Lys Ala Lys Glu Ile Ile Leu Ser Lys Leu 225 235 240 Asp Glu Glu Lys Leu Thr Lys Leu Gly Glu Leu Met Asn Ile Asn 245 250 255 His Gly Leu Leu Asp Ala Leu Gly Val Ser Thr Lys Lys Leu Gly Glu 260 265 270 Leu Val Tyr Ala Ala Arg Thr Ala Gly Ala Ile Gly Ala Lys Leu Thr 275 280 285 Gly Ala Gly Gly Gly Cys Met Tyr Ala Leu Ala Pro Gly Arg Gln 290 295 300

Arg Glu Val Ala Thr Ala Ile Lys Ile Ala Gly Gly Ile Pro Met Ile 305 310 315 320

Thr Arg Val Ser Arg Glu Gly Leu Arg Ile Glu Glu Val Ser Arg 325 330 335

<210> 10

<211> 334

<212> PRT

<213> Pyrococcus furiosus

<400> 10

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His Ser Val Val Tyr Gly Lys Pro Ala Ile Ala Ala Ile Asp Leu 20 25 30

Arg Thr Phe Val Glu Ala Glu Leu Ile Arg Glu Lys Lys Ile Arg Ile 35 40 45

Glu Ala His Asp Ile Lys Val Pro Gly Leu Thr Val Ser Phe Ser Glu 50 55 60

Asn Glu Ile Tyr Phe Glu Thr Asp Tyr Gly Lys Ala Ala Glu Val Leu 65 70 75 80

Ser Tyr Val Arg Glu Ala Ile Asn Leu Val Leu Glu Glu Ala Asp Lys 85 90 95

Lys Asn Val Gly Ile Lys Val Ser Ile Thr Ser Gln Ile Pro Val Gly 100 105 110

Ala Gly Leu Gly Ser Ser Ala Ala Val Ala Val Ala Thr Ile Gly Ala 115 120 125

Val Ser Lys Leu Leu Gly Leu Glu Leu Ser Lys Glu Glu Ile Ala Lys 130 135 140

Met Gly His Lys Thr Glu Leu Leu Val Gln Gly Ala Ser Ser Gly Ile 145 150 155 160

Asp Pro Thr Val Ser Ala Ile Gly Gly Phe Ile Phe Tyr Glu Lys Gly 165 170 175

Lys Phe Glu His Leu Pro Phe Met Glu Leu Pro Ile Val Val Gly Tyr 180 185 190

Thr Gly Ser Ser Gly Pro Thr Lys Glu Leu Val Ala Met Val Arg Lys 195 200 205

Arg Tyr Glu Glu Met Pro Glu Leu Ile Val Pro Ile Leu Glu Ala Met 210 215 220

Gly Lys Val Val Glu Lys Ala Lys Asp Val Ile Leu Ser Asn Val Asp 225 230 235 240

Lys Glu Glu Lys Phe Glu Arg Leu Gly Val Leu Met Asn Ile Asn His 245 250 255

Gly Leu Leu Asp Ala Leu Gly Val Ser Thr Lys Lys Leu Ser Glu Leu 260 265 270

Val Tyr Ala Ala Arg Val Ala Gly Ala Leu Gly Ala Lys Ile Thr Gly 275 280 285

Ala Gly Gly Gly Cys Met Tyr Ala Leu Ala Pro Asn Lys Gln Arg 290 295 300

Glu Ile Ser Arg Glu Gly Leu Lys Ile Glu Glu Val Ile Lys 325 330

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His Ala Val Val Tyr Ser Lys Pro Ala Ile Ala Ala Ile Asp Arg 20 25 30

Arg Val Thr Val Thr Val Ser Glu Ser Ser Ser Thr His Val Thr Ile 35 40 45

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Leu Asp Tyr Ile Gly Arg Cys Leu Glu Leu Tyr His Asp Ala Ser Pro 65 70 75 80

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<211> 303

<212> PR

<213> Methanobacterium thermoautotrophicum

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Ser Ser Ala Ala Leu Thr Val Ala Leu Ile Gly Ala Leu Asp Arg Tyr 100 105 110

His Gly Arg Asp His Gly Pro Gly Glu Thr Ala Ala Arg Ala His Arg 115 120 125

Val Glu Val Asp Val Gln Gly Ala Ala Ser Pro Leu Asp Thr Ala Ile 130 135 140

Ser Thr Tyr Gly Gly Leu Val Tyr Leu Asp Ser Gln Arg Arg Val Arg 145 150 155 160

Gln Phe Glu Ala Asp Leu Gly Asp Leu Val Ile Ala His Leu Asp Tyr 165 170 175

Ser Gly Glu Thr Ala Arg Met Val Ala Gly Val Ala Glu Arg Phe Arg 180 185 190

Arg Phe Pro Asp Ile Met Gly Arg Ile Met Asp Thr Val Glu Ser Ile 195 200 205

Thr Asn Thr Ala Tyr Arg Glu Leu Leu Arg Asn Asn Thr Glu Pro Leu 210 220

Gly Glu Leu Met Asn Leu Asn Gln Gly Leu Leu Asp Ser Met Gly Val 225 230 235 240

Ser Thr Arg Glu Leu Ser Met Met Val Tyr Glu Ala Arg Asn Ala Gly 245 250 255

Ala Ala Gly Ser Lys Ile Thr Gly Ala Gly Gly Gly Ser Ile Ile 260 265 270

Ala His Cys Pro Gly Cys Val Asp Asp Val Val Thr Ala Leu Asn Arg 275 280 285

Asn Trp Lys Ala Met Arg Ala Glu Phe Ser Val Lys Gly Leu Ile 290 295 300

<210> 12

<211> 284

<212> PRT

<213> Archaeoglobus fulgidus

<400> 12

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Cys Ile Phe Gly Leu Phe Lys Gly Glu Lys Pro Lys Gly Ser Phe Ile 260 265 270

Val Glu Pro Glu Lys Glu Gly Val Arg Ile Glu Glu 275 280

<210> 13

<211> 312 <212> PRT

<213> Methanococcus jannaschii

<400> 13

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Val Val Tyr Gly Tyr Arg Ala Ile Ser Met Ala Ile Asp Leu Thr Ser 20 25 30

Thr Ile Glu Ile Lys Glu Thr Gln Glu Asp Glu Ile Ile Leu Asn Leu 35 40 45

Asn Asp Leu Asn Lys Ser Leu Gly Leu Asn Leu Asn Glu Ile Lys Asn 50 60

Ile Asn Pro Asn Asn Phe Gly Asp Phe Lys Tyr Cys Leu Cys Ala Ile 65 70 75 80

Lys Asn Thr Leu Asp Tyr Leu Asn Ile Glu Pro Lys Thr Gly Phe Lys 85 90 95

Ile Asn Ile Ser Ser Lys Ile Pro Ile Ser Cys Gly Leu Gly Ser Ser 100 105 110

Ala Ser Ile Thr Ile Gly Thr Ile Lys Ala Val Ser Gly Phe Tyr Asn 115 120 125

Lys Glu Leu Lys Asp Asp Glu Ile Ala Lys Leu Gly Tyr Met Val Glu 130 135 140

Lys Glu Ile Gln Gly Lys Ala Ser Ile Thr Asp Thr Ser Thr Ile Thr 145 150 155 160

Tyr Lys Gly Ile Leu Glu Ile Lys Asn Asn Lys Phe Arg Lys Ile Lys 165 170 175

Gly Glu Phe Glu Glu Phe Leu Lys Asn Cys Lys Phe Leu Ile Val Tyr 180 185 190 Page 20

Ala Glu Lys Arg Lys Lys Thr Ala Glu Leu Val Asn Glu Val Ala 195 200 205

Lys Ile Glu Asn Lys Asp Glu Ile Phe Lys Glu Ile Asp Lys Val Ile 210 220

Asp Glu Ala Leu Lys Ile Lys Asn Lys Glu Asp Phe Gly Lys Leu Met 225 230 235 240

Thr Lys Asn His Glu Leu Leu Lys Lys Leu Asn Ile Ser Thr Pro Lys 245 250 255

Leu Asp Arg Ile Val Asp Ile Gly Asn Arg Phe Gly Phe Gly Ala Lys 260 265 270

Leu Thr Gly Ala Gly Gly Gly Cys Val Ile Ile Leu Val Asn Glu 275 280 285

Glu Lys Glu Leu Leu Lys Glu Leu Asn Lys Glu Asp Val Arg 290 295 300

Ile Phe Asn Cys Arg Met Met Asn

<210> <211>

14 324

PRT

Aeropyrum pernix

<400>

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Gly Glu His Phe Val Val Arg Gly Ser Leu Ala Ile Val Ala Ala Ile 20 25 30

Gly Arg Arg Leu Arg Val Thr Val Arg Ser Gly Gly Lys Gly Ile Val 35 40 45

Leu Glu Ser Ser Met Leu Gly Arg His Ser Ala Pro Leu Pro Gly Gln 50 60

Gly Ala Ala Lys Val Ser Pro Val Leu Glu Pro Tyr Ile Ala Val 65 70 75 80

Leu Arg Ser Leu Ala Ala Arg Gly Tyr Ser Val Val Pro His Thr Ile 85 90 95 Page 21

Leu Val Glu Ser Gly Ile Pro Pro Arg Ala Gly Leu Gly Ser Ser Ala 100 105 110

Ala Ser Met Val Ala Tyr Ala Leu Ser Tyr Ser Ala Met His Gly Asp 115 120 125

Pro Leu Ser Ala Glu Asp Leu Tyr Ser Val Ala Met Glu Gly Glu Lys 130 135 140

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Gly Gly Val Leu Ala Tyr Arg Arg Gly Glu Asn Pro Val Asp Ile Arg 165 170 175

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Leu Lys His Gly Lys Ala Gly Pro Ile Asp Ala Ala Ser Val Val Arg 195 200 205

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